REMARKS

Applicants thank Examiner Woitach for the interview granted August 10, 2005 and submit the present amendments and declaration in response to that interview.

Amendments

By the present amendment, claim 1 has been amended, as suggested by the Examiner, to add the active step of permeabilizing the mammalian cell, a step that finds support throughout the specification, for example, at page 46, lines 16-30; page 49, line 26 - page 50, line 15; and page 55, lines 12-29. Claim 1 has been further amended to replace the term "mitotic cell extract" with the equivalent term "extract from a mitotic cell" for the purpose of clarification. This amendment also finds support throughout the specification, for example, at page 36, line 22 – page 38, line 22, where the production of extracts from mitotic cells is exemplified. Claims 4, 6, and 43 have been amended to conform their language with that of amended claim 1. Claim 15 has been amended to correct a spelling and grammatical error. Withdrawn claims 16-42 have been canceled.

In addition, Applicants' priority claim to parent application, USSN 60/258,151, has been withdrawn.

No new matter is added by any of the amendments, and Applicants reserve the right to pursue all canceled subject matter in this or a future, related application.

Rejections under 35 U.S.C. § 102

Applicants acknowledge the withdrawal of the rejections under 35 U.S.C. § 102, as indicated during the interview of August 10, 2005 and in the Examiner's Interview Summary of August 12, 2005.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 4-15, and 43-53 stand rejected under 35 U.S.C. § 112, first paragraph as

lacking a written description, and claims 45-50 as lacking a written description and enablement.

As discussed at the interview and as indicated in the Examiner's Interview Summary, many aspects of this rejection are overcome by removal of the term "addition of a factor" from the present claims.

As further discussed during that interview, the present scope of the claims is appropriate from both a written description and enablement perspective as evidenced by the fact that the claimed method can be carried out routinely and reproducibly using mitotic extracts and the technique can be carried out successfully using extracts and permeabilized cells from any number of different species.

On the first issue relating to the use of a "mitotic cell extract" (or "extract from a mitotic cell," as the claims now read), the Office expressed initial concern regarding the question of whether Applicants' extracts were functional or whether an extract must be prepared from cells isolated at a particular stage of mitosis. As discussed at the interview and as stated in the accompanying Declaration from Dr. James M. Robl, this concern is unwarranted. As attested to by Dr. Robl, the cell cycle is typically divided into two general stages: mitosis and interphase. During mitosis, chromatin condensation and nuclear envelope breakdown occur, the events that appear to facilitate the enhanced efficiency of the present cloning method and that are required by the present claims. As discovered by Applicants, cell populations isolated in mitosis, and without further isolation based on cell stage, reproducibly trigger those events of chromatin condensation and nuclear envelope breakdown and have been used for the successful cloning of a variety of mammalian species.

As indicated by Dr. Robl in the accompanying Declaration, mitotic cells are routinely isolated in his laboratory at Hematech LLC by the technique generally described in the present specification at page 36, lines 23-26 and extracts prepared as generally described in the specification at page 36, line 28 – page 37, line 27. As stated by Dr.

Robl, such extract preparation has been carried out at least 75 independent times in his laboratory and is currently carried out by technician level scientists. When tested, these extracts are found to reproducibly trigger chromatin condensation and nuclear envelope breakdown. As stated by Dr. Robl, extracts at Hematech are typically tested by visual assessment for chromatin condensation as described in the specification, for example, at page 30, lines 29-30. In these tests, Applicants have determined that essentially 100% of the mitotic extracts assayed are functional.

In addition, as further attested to by Dr. Robl in the accompanying Declaration, these mitotic cell extracts reproducibly result in the cloning of desired mammals. At Hematech, this technique has been used to clone at least 25,000 bovine embryos, and, as indicated in more detail below, has been used by others to clone mammals of species as diverse as pigs and cats. In each case, mitotic cell extracts have been successfully utilized in these endeavors.

The second issue raised by the Office was the question of whether Applicants' technique was efficacious for mammalian cloning across a broad range of cell types and species. As indicated by Dr. Robl, functional mitotic extracts have been generated from both primary and cultured cells, in particular, primary bovine fetal fibroblasts as well as cultured Madin Darby bovine kidney cells and cultured Madin Darby canine kidney cells. Extracts have also been generated and used successfully from a broad range of species that include bovines, canines, and humans. All of these extracts were shown to trigger chromatin condensation and nuclear envelope breakdown.

Furthermore, these extracts triggered these events in an apprarently non-species-specific manner. As indicated by Dr. Robl, bovine mitotic extracts have been demonstrated to trigger chromatin condensation and nuclear envelope breakdown in bovine fibroblasts, bovine trophectodermal cells, and bovine placental cells, as well as porcine fetal fibroblasts, canine fibroblasts, and monkey fibroblasts. These results indicate that a mitotic extract from one species can be used to clone other species and that

this is true with respect to species as diverse as cows, pigs, dogs, and monkeys.

Further, as attested to in the Robl Declaration, consistent with this broad range of cell types and species amenable to Applicants' cloning approach, the technique has been used by Applicants or others to successfully generate cloned fetuses from cows, pigs, and cats, and for research to clone monkeys.

Due to its success, Applicants' technique and its inventor Dr. Robl have received widespread recognition in the scientific and popular press. For example, the success of the present technique has been published in articles in the prestigious, peer-reviewed journals, *Nature Genetics* and *Biology of Reproduction* (copies enclosed). In addition, the use of Applicants' technique to clone domestic cats has been reported on television and the internet by MSNBC.

In view of the above, Applicants request reconsideration on the remaining claim scope issues. Applicants' experimental results clearly demonstrate that mitotic cell extracts prepared as described in the present specification and without further isolation as to cell stage are efficacious in the claimed method. In addition, there can be no question that Applicants' technique facilitates the successful cloning of a wide variety of mammals using a broad range of cell types and cell species. Applicants have demonstrated that the present claim scope is appropriate, and the remaining rejections under 35 U.S.C. § 112, first paragraph should be withdrawn.

Rejection Based on Double Patenting

Claims 1, 4-15, and 43-53 also stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending applications, Robl (2004/0068760) and Collas (2002/0142397). As the claims of these copending applications have not yet been allowed or issued, Applicants

request withdrawal of this rejection upon an indication of otherwise allowable subject matter in the present case, as required by MPEP 822.[1]

Information Disclosure Statements

Applicants draw the Examiner's attention to the Information Disclosure Statement submitted July 11, 2005 and the Information Disclosure Statement filed herewith, and request consideration of the cited references and return to Applicants of the initialed Forms PTO-1449 with the Office's next communication in this case.

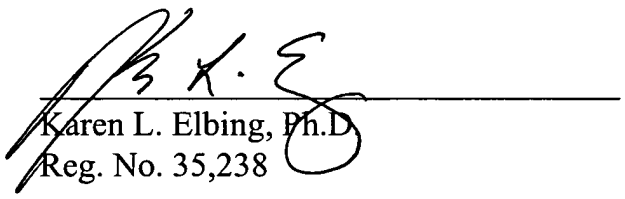
CONCLUSION

Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 11 October 2006



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[1] MPEP 822 states, in part, "The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent..."